McKusick-Kaufman syndrome

McKusick-Kaufman syndrome is a condition that affects the development of the hands and feet, heart, and reproductive system. It is characterized by a combination of three features: extra fingers and/or toes (polydactyly), heart defects, and genital abnormalities.

Most females with McKusick-Kaufman syndrome are born with a genital abnormality called hydrometrocolpos, which is a large accumulation of fluid in the pelvis. Hydrometrocolpos results from a blockage of the vagina before birth, which can occur if part of the vagina fails to develop (vaginal agenesis) or if a membrane blocks the opening of the vagina. This blockage allows fluid to build up in the vagina and uterus, stretching these organs and leading to a fluid-filled mass. Genital abnormalities in males with McKusick-Kaufman syndrome can include placement of the urethral opening on the underside of the penis (hypospadias), a downward-curving penis (chordee), and undescended testes (cryptorchidism).

The signs and symptoms of McKusick-Kaufman syndrome overlap significantly with those of another genetic disorder, Bardet-Biedl syndrome. Bardet-Biedl syndrome has several features that are not seen in McKusick-Kaufman syndrome, however. These include vision loss, delayed development, obesity, and kidney (renal) failure. Because some of these features are not apparent at birth, the two conditions can be difficult to tell apart in infancy and early childhood.

Frequency

This condition was first described in the Old Order Amish population, where it affects an estimated 1 in 10,000 people. The incidence of McKusick-Kaufman syndrome in non-Amish populations is unknown.

Genetic Changes

Mutations in the *MKKS* gene cause McKusick-Kaufman syndrome. This gene provides instructions for making a protein that plays an important role in the formation of the limbs, heart, and reproductive system. The protein's structure suggests that it may act as a chaperonin, which is a type of protein that helps fold other proteins. Proteins must be folded into the correct 3-dimensional shape to perform their usual functions in the body. Although the structure of the MKKS protein is similar to that of a chaperonin, some recent studies have suggested that protein folding may not be this protein's primary function. Researchers speculate that the MKKS protein also may be involved in transporting other proteins within the cell.

The mutations that underlie McKusick-Kaufman syndrome alter the structure of the MKKS protein. Although the altered protein disrupts the development of several parts of the body before birth, it is unclear how *MKKS* mutations lead to the specific features of this disorder.

Inheritance Pattern

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

Other Names for This Condition

- HMCS
- Hydrometrocolpos, postaxial polydactyly, and congenital heart malformation
- Kaufman-McKusick syndrome
- MKS

Diagnosis & Management

Genetic Testing

- Genetic Testing Registry: McKusick Kaufman syndrome
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C0948368/

Other Diagnosis and Management Resources

- GeneReview: McKusick-Kaufman Syndrome
  https://www.ncbi.nlm.nih.gov/books/NBK1502
- MedlinePlus Encyclopedia: Polydactyly
  https://medlineplus.gov/ency/article/003176.htm

General Information from MedlinePlus

- Diagnostic Tests
  https://medlineplus.gov/diagnostictests.html
- Drug Therapy
  https://medlineplus.gov/drugtherapy.html
- Genetic Counseling
  https://medlineplus.gov/geneticcounseling.html

- Palliative Care
  https://medlineplus.gov/palliativecare.html
- Surgery and Rehabilitation
  https://medlineplus.gov/surgeryandrehabilitation.html

Additional Information & Resources

MedlinePlus

- Encyclopedia: Polydactyly
  https://medlineplus.gov/ency/article/003176.htm
- Health Topic: Congenital Heart Defects
  https://medlineplus.gov/congenitalheartdefects.html

Genetic and Rare Diseases Information Center

- McKusick Kaufman syndrome
  https://rarediseases.info.nih.gov/diseases/3427/mckusick-kaufman-syndrome

Additional NIH Resources

- National Human Genome Research Institute: Gene Linked to Developmental Syndrome in Old Order Amish Identified by NIH Scientists
  https://www.genome.gov/10001484/

Educational Resources

- Cleveland Clinic: Congenital Hand Differences
  http://my.clevelandclinic.org/health/articles/congenital-hand
- Disease InfoSearch: McKusick Kaufman syndrome
  http://www.diseaseinfosearch.org/McKusick+Kaufman+syndrome/4529
- MalaCards: mckusick-kaufman syndrome
  http://www.malacards.org/card/mckusick_kaufman_syndrome
- March of Dimes: Genital and Urinary Tract Defects
  http://www.marchofdimes.org/baby/genital-and-urinary-tract-defects.aspx
- Orphanet: McKusick-Kaufman syndrome
  http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=2473

Patient Support and Advocacy Resources

- American Heart Association
  http://www.heart.org/HEARTORG/Conditions/CongenitalHeartDefects/Congenital-Heart-Defects_UCM_001090_SubHomePage.jsp

GeneReviews

- McKusick-Kaufman Syndrome
  https://www.ncbi.nlm.nih.gov/books/NBK1502

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28mckusick-kaufman+syndrome%5BTIAB%5D%29+OR+%28kaufman-mckusick+syndrome%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D

OMIM

- MCKUSICK-KAUFMAN SYNDROME
  http://omim.org/entry/236700

Sources for This Summary

- David A, Bitoun P, Lacombe D, Lambert JC, Nivelon A, Vigneron J, Verloes A. Hydrometrocolpos and polydactyly: a common neonatal presentation of Bardet-Biedl and McKusick-Kaufman syndromes. J Med Genet. 1999 Aug;36(8):599-603.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/10465109
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1762973/
- GeneReview: McKusick-Kaufman Syndrome
  https://www.ncbi.nlm.nih.gov/books/NBK1502
- Slavotinek AM, Biesecker LG. Phenotypic overlap of McKusick-Kaufman syndrome with bardet-biedl syndrome: a literature review. Am J Med Genet. 2000 Nov 27;95(3):208-15. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/11102925
- Stone DL, Slavotinek A, Bouffard GG, Banerjee-Basu S, Baxevanis AD, Barr M, Biesecker LG. Mutation of a gene encoding a putative chaperonin causes McKusick-Kaufman syndrome. Nat Genet. 2000 May;25(1):79-82.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/10802661

Reprinted from Genetics Home Reference:
https://ghr.nlm.nih.gov/condition/mckusick-kaufman-syndrome

Reviewed: May 2008
Published: March 21, 2017

Lister Hill National Center for Biomedical Communications
U.S. National Library of Medicine
National Institutes of Health
Department of Health & Human Services